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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/728,195	12/03/2003	Shan Lu	07917-0269001/UMMC 03-24	7308

26161 7590 08/27/2009

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EXAMINER	
PENG, BO	

ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
08/27/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/728,195	LU ET AL.	
	Examiner	Art Unit	
	BO PENG	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *54,55,57-60,81-85,88,94,96,100,107,115-117 and 119-123* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54, 55, 57-60, 81-85, 88, 94, 96, 100, 107 and 115-117 and 119-123* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office action is in response to the amendment filed April 30, 2009. Claims 1-53, 56, 61-80, 86, 87, 89-93, 95, 97-99, 101-106, 108-114, and 118 have been cancelled. New Claim 123 has been added. Accordingly, Claims 54, 55, 57-60, 81-85, 88, 94, 96, 100, 107, 115-117 and 119-123 are pending, and are considered in this Office action.

Claim Rejections - 35 USC § 112, second paragraph

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. (**New objection**) New Claim 123 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Claim 123 recites: "The method of Claim 54, wherein the sets of nucleic acid molecules encode wild-type HIV envelope gpl20 glycoproteins from primary isolates A, B715, Ba-L, Czm, and E, ..." It is not clear if the applicant intends Claim 123 to mean "isolates A, ... and E" , or "a primary isolate" from clade A, ...and clade E. It is noted that "primary isolates A, ... and E" of Claim 123 are not defined by the specification. Please note in the HIV art that "an isolate" means a strain (species) of HIV, while "a clade" means "a group of organisms (subgenus) comprising all the evolutionary descendants of a common ancestor". Since the specification has failed to define primary isolates A and E, one of ordinary skill in the art is not able to reasonably apprise the scope of the invention.

Claim Rejections - 35 USC § 112-WD

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. (**Prior rejection-withdrawn**) The rejection of Claims 54, 55-60, 81-85, 88, 94, 96, 100, 107 and 115-122 under 35 U.S.C. 112, first paragraph, as containing NEW Matter, **is withdrawn** in view of the amendment to the claims.

7. (**New rejection-necessitated by the amendment**) Claim 123 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

8. Please note that "... wild-type HIV envelope gpl20 glycoproteins from primary isolates A, ... and E, ..." recited in Claim 123 is NEW MATTER. There is no support for the new limitation of "primary isolates A and E" in the specification. Also see the rejection under 35 USC § 112, second paragraph, set forth above. Removal of all new matter is required. Reference: In re Russsmussen 210 USPQ 325.

Claim Rejections - 35 USC § 112-Scope of Enablement

9. (**New rejection-necessitated by the amendment**) Claims 54, 55, 57-60, 81-85, 88, 94, 96, 100, 107,115-117 and 119-123 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inducing an immune response to an HIV epitope in human, does not reasonably provide enablement

for a method of inducing a protective immune response against a current or future HIV infection in humans. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth.

"[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *Genentech Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also *Amgen Inc. v. Chugai Pharm. Co.,* 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* [230 USPQ 546, 547 (BdPatAppInt 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d

1510, 1513 (Fed. Cir. 1993).

10. *Breadth of the claims.* The claims have been amended to be directed to a method of inducing **a protective immune response against a current or future HIV infection in human** comprising prime immunizing a human with (a) a set of HIV envelope DNAs and (b) a set of HIV gag DNAs, and boost immunizing **a human** with a set of HIV envelope proteins of different clades. The specification (Para [0024]) defines:

"Methods and compositions described herein cover a nucleic acid, e.g., DNA plasmid, vaccine that induces humoral (e.g., neutralizing antibody) responses and/or cell-mediated immune response (e.g., cytotoxic T lymphocyte (CTL)) responses in the recipient as **protection against current or future HIV (e.g., HIV-1) infection**. **The vaccine can induce protection against infection upon subsequent challenge with HIV. Protection refers to resistance (e.g., partial resistance) to persistent infection of a host animal with HIV**. Neutralizing antibodies generated in the vaccinated host can provide this protection. In other situations, CTL responses can provide this protection. In some situations, both neutralizing antibodies and cell-mediated immune (e.g., CTL) responses provide this protection.

Thus, as indicated by both the claims and the specification, the claimed method is directed to inducing a protective immune response against a current or future HIV infection in human, providing protection against infection upon subsequent challenge with HIV, wherein the protection refers to resistance (e.g., partial resistance) to persistent infection of the host animal with HIV.

11. *Working examples.* In supporting the claims, Applicants submitted post-filing Wang reference (Vaccine 26:3947-3957, 2008, Exhibit A), which shows that, in a Phase I clinical trial, the vaccine formulation DP6-001 can induce HIV-1-specific immune responses in healthy adult volunteers. DP6-001 comprises polyvalent DNA plasmids and proteins as recited in the claims. Wang states: "Robust cross-subtype HIV-l-specific T cell responses were detected in IFN ELISPOT assays. Furthermore, we detected high titer

serum antibody responses that recognized a wide range of primary HIV-1 Env antigens and also neutralized pseudotyped viruses that express the primary Env antigens from multiple HIV-1 subtypes" (see Abstract). However, it is noted that Wang does not show whether or not the immune responses induced by the vaccine DP6-001 in human can "against a current or future HIV infection in human", or "induce protection against infection upon subsequent challenge with HIV", as defined by the specification Par [0024] recited above.

12. *Predictability of the art.* The art indicates that several forms of uncertainty exist as to whether the claimed method can induce a **protective immune response** against a current or future HIV infection in humans upon subsequent challenge with HIV. First, those of skill in the art recognize that a variety of artificial *in vitro* assays, such as neutralizing antibody assays, are generally used for detecting neutralizing antibodies. However, one of ordinary skill in the art also recognized that the neutralizing activity of an vaccine regiment detected in these *in vitro* assays is not generally correlated to its protective immunity in human, see e.g. Abstract, Fenyo (PLoS One. 2009;4(2):e4505) and Mann AM, *et al*. (AIDS.23:1659-1667, 2009). Moreover, the art also indicates that the current neutralizing antibody assays lack "uniformity in target strains used by different investigators to assess cross-neutralization has made the comparison of vaccine-induced antibody responses difficult", see e.g. Abstract, Li M, et al. J Virol. 2005 Aug;79(16):10108-25. Thus, it is not certain how the neutralizing activities detected in the *in vitro* assay translate to "a **protective immune response** against a current or future HIV infection in human upon subsequent challenge with HIV". In other words, it is not certain in the art how Applicants' neutralizing activities detected in the *in vitro* assay

correlate with its *in vivo* utility.

13. It is noted that Wang (Exhibit A) shows that the DP6-001 formulation only induce low or no cross neutralizing activity against primary HIV isolates included in Tier 2 in third neutralizing study (See Para 1, right col. p. 3952), Wang clearly shows that the DP6-001 formulation has not induced "a protective immune response that provides protection against a current or future infection with HIV" as Applicants claimed. Given that "there is enormous sequence heterogeneity among individual isolates of HIV-1" (Para 1, left col. p. 222, Desrosiers RC. Nature Medicine Vol. 10 (2004), it is unpredictable if neutralizing activities induced by DP6-001 could "provide protection against a current or future infection with HIV" as Applicants claimed.

14. The state of the art of HIV vaccine development indicates that it is extremely difficult to induce protective immune response against a current or future HIV infection in human upon subsequent challenge with HIV, see Desrosiers RC. Nature Medicine Vol. 10 (2004), pp. 221-223), and Haynes (J. Allergy Clin Immunol. 2008;122:3-9, 2008). Up to now, HIV vaccines have not proved to be effective for their intended purpose due to the well-known difficulties inherent in development of HIV vaccines. Some of those problems are outlined here: 1) the extensive genomic diversity associated with the HIV retrovirus; 2) the existence of latent forms of the virus; 3) the ability of the virus to "immune escape" from natural and adoptive immunity against the virus, etc., Several clinical trials have been conducted to date, but in every situation, the immunogen failed to induce protective immunity, failed to control viremia, and failed to protect individuals at a high risk from infection. Moreover, no experimental vaccine candidates so far have been proven to be effective to protect monkeys from SIV infection in animal models.

Thus, it is not predictable in the art if the claimed method can induce a **protective immune response** against a current or future HIV infection in human upon subsequent challenge with HIV. Desrosiers RC states: "The inability to solve fundamental scientific questions is the root cause for why a successful vaccine is not currently with our grasp" (Nature Medicine Vol. 10 (2004), pp. 221-223). Thus, given the current state of the art of HIV vaccine development, it is unpredictable if the immune responses induced by the vaccine DP6-001 in human can "protect against a current or future HIV infection in human", or "induce protection against infection upon subsequent challenge with HIV".

15. *Amount of experimentation necessary*. Since the claimed invention is directed to a method of inducing **a protective immune response against current or future HIV infection in humans**, and in view of the empirical and unpredictable nature of the invention with regard to induction of protective immunity inhibiting HIV infection in humans, one skilled in the art cannot practice the claimed invention without undue experimentation. Therefore, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. (**Prior rejection-maintained**) The rejection of Claims 54, 55, 57-60, 81-85, 88, 94, 96, 100, 107, 111-117 and 119-122, under 35 U.S.C. 103(a) as being unpatentable over Barnett (Vaccine, Vol. 15 (1997), No. 8, pp 869-873), Nabel (WO 02/032943, International filing date August 14, 2001; and International Publication date April 25, 2002); Gao L (*J. Virology* Vol.70 (1996), No.3, pp 1651-1667); Gao F. *et al.* (Meeting Abstract; *AIDS Vaccine 2001.* 2001 Sep 5-8; abstract no. 201); Yoshida T. *et al.* Clin Exp Immunol. 2001 Jun;124(3):445-52; and Evans (Vaccine. 2001 Feb 28;19(15-16):2080-91), is **maintained** and **restated**. It is noted that claims have been amended to be directed to a method of inducing a protective immune response in **humans** comprising prime immunizing the mammal with (a) a set of HIV envelope DNAs and (b) a set of HIV gag DNAs, and boost immunizing **the subject** with a set of HIV envelope proteins of different clades, wherein one of more DNA vaccines comprise optimized codons. Although the cited references do not explicitly teach administering DNA and/or protein vaccines to a human, the cited references are still relevant to the claimed method. All cited references teach methods of inducing immune responses against HIV (human), although the DNA and/or protein vaccines are tested in animal models. As indicated in the previous Office action, Barnett teaches the active steps of the claimed method: DNA priming (step 54a) and protein boosting immunization (step 54b). All the compositions of HIV env and gag used in the claimed method have been disclosed by the cited references, see Nabel, Gao and Yoshida. Use a combination of HIV Clades A to G as multiple (or polyvalent) vaccine compositions is also explicitly suggested by the cited Barnett and Nabel references. Barnett also teaches that neutralizing antibody activity is detected after the gp120 protein boost, see e.g. Abstract, and bridging Para between p. 871-872. Thus,

in view of the combined teaching and success of the cited references, one of ordinary skill in the art would have a reasonable expectation of success in inducing a protective immune response against an HIV epitope in humans using the approach and the compositions taught by the prior art references.

In response to Applicants' arguments:

18. First, by initially attacking the cited references, Applicants argue that the cited references do not teach or suggest the specific combination of DNA and protein vaccines recited in the claims as presently amended.

19. This argument is not persuasive. It is noted that this is an obviousness type rejection. Thus, the precise limitations of the present claims need not be specifically identified in the present claims if they represent obvious variations of the co-pending claims. Therefore, since this argument is based on targeting the cited references individually, it is not found persuasive.

20. Secondly, Applicants argue that none of the cited references teaches any successful efforts at obtaining a protective immune response, e.g. in the form of neutralizing antibodies in human. Applicants assert that “a protective immune response is one that provides protection against a current or future infection with HIV. Thus, a protective immune response is more than just any immune response”. Many researchers have been able to generate an immune response, e.g., raising antibodies, by vaccination with a DNA-based vaccine, but few have raised "neutralizing" antibodies in animal models, and no one prior to the applicants has been able to raise such neutralizing

antibodies that inhibit the HIV viruses from replicating and/or proliferating in human subjects". Specifically, Applicants argues that Nabel's group has shown that "[n]o neutralizing antibody was detected" in their human clinical studies, see Catanzaro *et al.*, *J. Infectious Dis.,* 194:1638-1649 (2006)(**Exhibit B**).

21. This argument is considered, but found not persuasive. Applicants' argument based on "neutralizing antibody" is not relevant to the claims. Applicants are arguing a limitation that is not in the claims. The claims do not limit "a protective immune response to only a neutralizing antibody. The instant specification Para [0024] indicates that not only a neutralizing antibody, but also CTL, provides protective immune responses. The specification Para [0024] recites: "In other situations, CTL responses can provide this protection. In some situations, both neutralizing antibodies and cell-mediated immune (e.g., CTL) responses provide this protection". With regard to Nabel's vaccine study, Exhibit B clearly shows that CTL responses were induced in vaccine recipients, see e.g. Abstract. Moreover, Applicants are apparently comparing different vaccine formulations. As Applicant indicated in Para line 6, p. 15, Remarks, Nabel's vaccine regiment does not include a "protein boost". One of ordinary skill in the art knows that a protein (or subunit) vaccine can induce an antibody response. As shown by Barnett, serum neutralizing antibodies against HIV are substantially increased in DNA immunized animals following a single boost with recombinant go120 protein subunit, see e.g. Abstract. Thus, it is not unexpected that Nabel's group didn't show their DNA vaccine regiment produced neutralizing antibody. Thus, Applicants' argument and study comparison based only on "neutralizing antibody" is not relevant to the claims and misleading.

22. Finally, Applicants argue that Wang (Exhibit A) has shown surprising results in a human clinical trial, in which applicants have been successful in inducing neutralizing antibodies against multiple HIV subtypes in human volunteers. As evidence, Applicants recite following paragraph form Wang (Exhibit A):

"High-titer NAb [neutralizing antibody] responses (up to 1:2147) were identified in all human immune sera against the **three sensitive viruses [MN, NIA-3, and SF162]** (Fig. 3b). Using a NAb titer of 1:20 as the cut-off, more than 50% of vaccines also showed positive neutralizing activities against eight pseudotyped viruses [of subtypes A, B, C, D, and E], while the three remaining pseudotyped viruses ... were more resistant to neutralization (Fig. 3c)" (p. 3952, left col., last two lines, to right col., line 8).

"The DP6-001 formulation elicited neutralizing activities against the sensitive viruses (TCLA and SF162) that **were comparable to or better than those elicited by recombinant gp120 alone** [30], and clearly much better than a recently reported DNA vaccine alone approach which did not show neutralizing antibody activities [14].

23. Exhibit A and Applicants argument are fully considered, but are not sufficient to overcome the 103 rejection. First, it is noted that while the Applicants have shown that neutralizing antibody activities have been detected in *in vitro* neutralizing assays, **these results are not commensurate with the scope of the claimed invention.** See e.g., MPEP 716.02(d). It is noted that claims require induction of "a protective immune response against a current or future infection with HIV". However, the art does not recognize that the neutralizing antibody activity detected by *in vitro* assay is equal to "a protective immune response against a current or future infection with HIV in human". See Para 12-14 above. Wang has not shown that the neutralizing antibody activity induced by vaccine DP6-001 can "protect against a current or future infection with HIV in humans" as Applicants claimed. Thus, Applicants' evidence provided by Wang (Exhibit A) is not commensurate with the scope of the claimed invention. Also see Para

5-14 above.

24. Secondly, the neutralizing antibody result shown in Exhibit A is not surprising as Applicants asserted. As recited above, Wang teaches: "The DP6-001 formulation elicited neutralizing activities against the sensitive viruses (TCLA and SF162) that **were comparable to or better than those elicited by recombinant gp120 alone** [30], and clearly much better than a recently reported DNA vaccine alone approach which did not show neutralizing antibody activities [14]". It is noted the cited reference [30] is Montefiori DC. Evaluating neutralizing antibodies against HIV, SIV and SHIV in luciferase reporter gene assays, ln: Coligan JE, Kruisbeek AM, Margulies DH, Shevach EM, Strober W. Coico R, editors. *Current protocols in immunology*. John Wiley & Sons; 2004. p. 12.1.1-5". Please note that "a protocol" generally means a general practice. Wang apparently teaches that the neutralizing activities induced by the DP6-001 formulation "were comparable to or better than those elicited by recombinant gp120 alone" as shown in *Current protocols in immunology*. Also, it is known in the art that some HIV strains, like MN, NL4-3, SF162, are highly sensitive stains to neutralization, see e.g. right co. p. 10114, and Para 2, p. 10116, Li M, *et al.* (J Virol. 79(16):10108-25, 2005). Thus, Wang clearly shows that neutralizing activities against the panel of Tier 1 HIV-1 viruses are comparable to or better than those elicited by recombinant gp120 alone. This is not considered as "surprising results".

25. Moreover, Wang shows that vaccine DP6-001 results in low neutralizing activities against the **standard** panel of Tier 2 HIV-1 viruses, which induce primary HIV isolates, in addition to sensitive viruses MN, NL4-3 and SF162. Wang recites:

"The neutralizing activities against the standard panel of Tier 2 HIV-1 viruses **were low in the current study, even at low serum dilutions**. While it is unclear whether this panel represents more resistant viruses than the viruses included in the other two neutralization assays, it is possible that the difference reflects the inclusion of more contemporary viral isolates in the Tier 2 panel while Env antigens included in the DP6-001 formulation were cloned from patient samples collected around or before the early 1990s. While the current DP6-001 formulation, **as a proof of concept study**, may not have the optimal profile to move to more advanced clinical trials, **the results included in this report clearly indicate that the use of a polyvalent, DNA prime-protein boost approach is feasible in order to elicit human neutralizing activities against a wide range of HIV-1**."

Thus, since the DP6-001 formulation only induces little or no cross neutralizing activity against primary HIV isolates included in Tier 2, Wang clearly shows that the DP6-001 formulation has not induced "a protective immune response "that provides protection against a current or future infection with HIV" as Applicants claimed.

26. For the reason discussed above, the rejection is maintained.

Remarks

No claim is allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the

Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bo Peng, Ph.D. whose telephone number is 571-272-5542. The examiner can normally be reached on Tu-F, 8:30-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/BO PENG/
Primary Examiner, Art Unit 1648